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NOTICE OF ALLOWANCE AND FEE(S) DUE

20583 7590 02/04/2010

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
HILL, MYRON G	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/04/2010

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,363	09/08/2003	James F. Young	10271-159-999	3135

TITLE OF INVENTION: ULTRA HIGH AFFINITY NEUTRALIZING ANTIBODIES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	05/04/2010

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

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NEW YORK, NY 10017

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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nonprovisional	NO	$1510	$300	$0	$1810	05/04/2010

EXAMINER	ART UNIT	CLASS-SUBCLASS
HILL, MYRON G	1648	424-147100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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EXAMINER	
HILL, MYRON G	
ART UNIT	PAPER NUMBER
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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 362 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 362 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

Notice of Allowability	Application No.	Applicant(s)	
	10/657,363	YOUNG ET AL.	
	Examiner	Art Unit	
	MYRON G. HILL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the papers filed 11/6/09*.

2. ☒ The allowed claim(s) is/are *86-117*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 11/6/09
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/M. G. H./
Examiner, Art Unit 1648

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Tamera Weisser on 1/7/10 and 1/27/010.

The application has been amended as follows:

114. The method of claim 86 or 87, wherein the Ka is 10^{10}-$\underline{M}^{-1}$.

115. The method of claim 88, wherein the Ka is 10^{10}-$\underline{M}^{-1}$

116. The method of claim 86 or 87, wherein the Ka is 10^{11}-$\underline{M}^{-1}$.

117. The method of claim 88, wherein the Ka is 10^{11}-$\underline{M}^{-1}$.

In the specification delete page 8 line 15 to page 10 line 14 and replace with the following which adds SEQ ID#s to Figures 1 and 3-7 to identify sequences found in the drawings:

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows the amino acid sequence of the light and heavy chain variable regions of an anti-RSV antibody wherein the CDR regions are underlined while non-underlined residues form the framework regions of the variable regions of each chain. In this antibody, the CDRs are derived from a mouse anti-RSV antibody while the framework regions consist mostly of sequences derived from a human antibody. For each CDR, locations at which amino acid replacements were used to achieve the high affinity CDRs and antibodies disclosed herein are in bold face. In accordance with the disclosure herein, such replacements were only in CDRs L2, L3, H1 and H3. FIG. 1A shows the light chain variable region (SEQ ID NO: 1) and FIG. 1B shows the heavy chain variable region (SEQ ID NO: 2) of the light and heavy chains, respectively. Constant region sequences are not shown. These sequences are present in the basic clone (see Table 2), designated IX-493 throughout this disclosure (i.e., SWSG--meaning a serine (S) at the key position (see tables 1 and 3) of high affinity CDR H1, a tryptophan (W) at the key position of high affinity CDR H3, a serine (S) at the key position of high affinity CDR L2, and a glycine (G) at the key position of high affinity CDR L3). For purposes of this disclosure, this is the "reference antibody."

FIG. 2 shows affinity comparisons for a particular set of beneficial or high affinity clones. The clonal designations are on the left of the legend at the right of the drawing along with the indicated substitutions at CDRs H1, H3, L2, and L3 shown on the right of the legend. Measurements are by ELISA (OD at 560 nm shown on the left axis). Clone L1FR represents the results for the reference antibody

structure of FIG. 1.

FIG. 3 shows the heavy (panel B--SEQ ID NO: 18) and light (panel A--SEQ ID NO: 17) chain variable regions for the preferred embodiment of clone 1 (Table 2) of the invention disclosed herein. CDR regions are underlined while the amino acid differences versus the antibody of FIG. 1 are indicated in bold face. Thus, this preferred (i.e., high affinity) antibody has several of the high affinity CDRs (Table 3) present which give rise to higher affinity (over 10.sup.10 M.sup.-1) than the basic or reference antibody.

FIG. 4 shows the heavy (panel B--SEQ ID NO: 20) and light (panel A--SEQ ID NO: 19) chain variable regions for the preferred embodiment of clone 2 (Table 2) of the invention disclosed herein. CDR regions are underlined while the amino acid differences versus the antibody of FIG. 1 are indicated in bold face. Thus, this preferred (i.e., high affinity) antibody has several of the high affinity CDRs (Table 3) present which give rise to higher affinity (over 10.sup.10 M.sup.-1) than the basic or reference antibody.

FIG. 5 shows the heavy (panel B--SEQ ID NO: 22) and light (panel A--SEQ ID NO: 21) chain variable regions for the preferred embodiment of clone 3 (Table 2) of the invention disclosed herein. CDR regions are underlined while the amino acid differences versus the antibody of FIG. 1 are indicated in bold face. Thus, this preferred (i.e., high affinity) antibody has several of the high affinity CDRs

(Table 3) present which give rise to higher affinity (over 10.sup.10 M.sup.-1) than the basic or reference antibody.

FIG. 6 shows the heavy (panel B--SEQ ID NO: 24) and light (panel A--SEQ ID NO: 23) chain variable regions for the most preferred embodiment of clone 22 (Table 4) of the invention disclosed herein. CDR regions are underlined while the amino acid changes versus the antibody of FIG. 1 are indicated in bold face. Thus, this most preferred (i.e., highest affinity) antibody has several of the high affinity CDRs (Table 3) present which give rise to higher affinity (over 10.sup.11 M.sup.-1) than the basic or reference antibody).

FIG. 7 shows the heavy (panel B--SEQ ID NO: 26) and light (panel A--SEQ ID NO: 25) chain variable regions for the preferred embodiment of clone 23 (Table 4) of the invention disclosed herein. CDR regions are underlined while the amino acid changes versus the antibody of FIG. 1 are indicated in bold face. Thus, this preferred (i.e., highest affinity antibody, has several of the high affinity CDRs (Table 3) present which give rise to higher affinity (over 10.sup.11 M.sup.-1) than the basic or reference antibody).

The following is an examiner's statement to state the availability of the recited antibody IX-493.

IX-493 is FAb fragment of MEDI-493, see specification page 11, lines 18-19. MEDI-493 is the same antibody as palivizumab, see Johnson et al. JID 1999 Vol 180, No 1, pages 35-40, from IDS). Palivizumab is the generic name for Synagis©. See package information inserts relating generic name to the brand name (from IDS, inserts dated 1999 and 2002, one page each).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MYRON G. HILL whose telephone number is (571)272-0901. The examiner can normally be reached on M-Th and flex.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher/
Primary Examiner, Art Unit 1648

/M. G. H./
Examiner, Art Unit 1648